REMARKS

Claims 1-9 and 25-29 are pending in this application. Claim 1 has been amended. Support for the amended claim comes from at least page 6, lines 1-4.

The following remarks are numbered to correspond to the numbering used in the referenced Office action.

3-4 The Provisional Obviousness Double Patenting Rejection

The Office has provisionally rejected claims 1-9 and 25-29 under the judicially created doctrine of obviousness type double patenting as being unpatentable of claims 1-7, 10-16, 20, 35-39 and 41-44 of copending application serial no. 09/183824.

No action is believed required by Applicant as the alleged conflicting claims have not in fact been patented.

5-6 The Rejection of the Claims Under 35 U.S.C. 112, First Paragraph

The Office has rejected claims 1-9 and 25-29 under 35 U.S.C. § 112, first paragraph. The Office alleges that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention at the time the application was filed. Specifically, the Office alleges the specification contains no written description supporting the recitation "G1 and G0" in claim 1 as amended and only supports G1 or G0. (Paper 17, page 3). The Office has directed Applicants' attention to page 14, second paragraph of the specification as supporting its contention. Applicants respectfully traverse.

It is well settled that a claim recitation need not be found, ibsis verbis, in an Applicants' specification in order that the written description requirement of 35 U.S.C. 112, first

paragraph be satisfied. A proper review focuses on whether or not a skilled artisan would understand by the description that the Applicant had possession of the claimed invention at the time the application was filed. Applicants direct the Office's attention to the specification at, for example, page 6, lines 1-4, which states"

> The composition is substantially free of glycoproteins comprising an immunoglobulin CH2 domain wherein the N-linked oligosaccharide is a G1 or G0 oligosaccharide. (emphasis supplied).

In view of the disclosure, a skilled artisan would understand that Applicant had possession of a preparation substantially free of glycoproteins containing G1 or G0 oligosaccharides.

Further, Applicants respectfully submit that the Office has applied a meaning to Applicants disclosure at page 14, second paragraph that would not be supported by the skilled artisan. The Office contends that the specification defines "by products" as "G0 and G1" and therefore the recitation of claim 1 "does not exceed 10% by weight" refers to amount of both G1 and G0 glycoforms together and not one or the other. (Paper 17, page 3). Applicants disagree and direct the Offices attention to the specification at page 14, second paragraph, which, in fact, states "substantially devoid of by-products originated from undesired glycoforms (e.g. G0 and G1). (emphasis supplied). Applicants description that the undesired glycoforms maybe, by way of example, G0 and G1 glycoforms would in no way imply to the skilled artisan (especially in view of the disclosure noted above) that undesired glycoforms could not be either G0 or G1.

It is respectfully submitted that the Office's position does not reflect Applicants' actual disclosure and moreover would not be read by a skilled artisan in the manner suggested by the Office. In view of the foregoing, Applicants submit that the claims are fully enabled by the specification as originally filed and respectfully request withdrawal of the pending rejection of the claims under 35 U.S.C. § 112 first paragraph.

4-5. The Rejection of the Claims under 35 U.S.C. 102(b)

The Office has rejected claims 1-5 and 25 under 35 U.S.C. 102(b) as being anticipated by Kumpel et al., (1994) Hum. Antib. Hybridomas 5(3 and 4):143-151 (Kumpel). The Office contends that Kumpel teaches human monoclonal antibodies wherein substantially all of the oligosaccharide is a G2 oligosaccharide referring to Table 1 and columns 1-3 at page 149 of Kumpel. The Office states that the preparations are substantially homogenous for the glycoprotein because they contain monoclonal antibodies in serum free tissue culture medium. The Office further contends that Applicant's claims and specification do not disclose the degree of purity associated with the term "substantially all." Applicants respectfully traverse.

As Applicants have previously noted, Kumpel describes a monoclonal antibody, 2B6, produced from an EBV-transformed B-lymphoblastoid cell line. Table 1 of Kumpel also shows that 21.7% of the oligosaccharides in the antibody preparation are sialylated (Table 1 and text at page 146). Kumpel also state that the 2B6 preparation contained the least amount of sialic acid of all the antibodies tested. Therefore, at least 21.7% of the oligosaccharides in each preparation are not G2 oligosaccharides meaning that none of the preparations described by Kumpel anticipate Applicants claim which requires a substantially homogenous G2 glycoform preparation.

Further, the Office has pointed to Table 1 to support its position that Kumpel describe antibody preparations wherein the G0 glycoform does not exceed 10% using the 2B6 or JAC10 or BRAD-3/LD antibodies of Kumpel as examples. However, it appears the Office has failed to recognize that the portion of Table 1 relied upon does not describe antibody preparations, rather, released oligosaccharides. Further the released oligosaccharides that Kumpel refers to under the heading "Asialo P4 profile" have been modified from how they appeared while on the antibody (Kumpel, page 144, last paragraph; age 145, first paragraph; page 146,

second paragraph). They are asialo forms of the oligosaccharide. Therefore, Kumpel does not anticipate an antibody preparation such as the one claimed by Applicant.

Further, Applicants disagree that the specification fails to define the degree of purity associated with the limitation "substantially all," as that term is clearly used in the context of the present invention to refer to a composition substantially free of glycoproteins comprising an immunoglobulin CH2 domain wherein the N-linked oligosaccharide is a G1 or G0 oligosaccharide (see, for example, page 6, lines 1-4) and, for example, page 14, lines 3-9,

> The phrases "substantially homogenous", "substantially uniform" and "substantial homogeneity" and the like are used to indicate that the product is substantially devoid of by-products originated from undesired glycoforms (*e.g.* G0 and G1). Expressed in terms of purity, substantial homogeneity means that the amount of by-products does not exceed 10%, and preferably is below 5%, more preferably below 1%, most preferably below 0.5%, wherein the percentages are by weight. (emphasis supplied)

In an effort to advance allowance of the subject matter of the claims, Applicants have amended claim 1 to delete reference to the term "substantially all".

In view of the foregoing Applicant request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(b).

6-7. The Rejection of the Claims under 35 U.S.C. 103(a)

The Office has rejected claims 1-9 and 25-29 under 35 U.S.C. 103(a) as being unpatentable over Kumpel, in view of US patent 5,834,251 by Maras et al. (Maras et al.). The Office contends that Kumpel teach that antibodies with substantially all G2 oligosaccharide have increased lysis of target cells in comparison the same antibody which is produced in a manner that results in low levels of G2. The Office further contends that Maras et al. teach that a galactosyltransferase enzyme can be

used to modify the oligosaccharide profile on a glycoprotein while relying on the specification for disclosure of clinical uses of various antibodies. Applicants respectfully traverse.

As discussed in the previous section, Kumpel do not describe or suggest a composition comprising a glycoprotein wherein substantially all of the oligosaccharide is a G2 oligosaccharide. Importantly, Kumpel do not describe increased lysis of target cells for an antibody after chemical removal of the sialic acid residues. The activity data described by Kumpel is for a heterogenous glycoprotein preparation and not a substantially homogenous preparation as claimed by Applicant. In fact, as described above almost 22 % of the galactosylated oligosaccharides detected by Kumpel terminated in a sialic acid residue. Therefore Kumpel alone or in combination with Maras et al. fail to provide the motivation to produce Applicant's claimed compositions but rather suggest only that some heterogenous glycoprotein preparation can be prepared. Further, there is no suggestion in Kumpel of how to achieve Applicants invention.

To view the combinations of disclosures to suggest a substantially homogenous preparation as claimed relies on impermissible hindsight analysis in view of the teaching offered only by Applicant since none of the describe or suggest a substantially homogenous preparation be prepared.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the pending rejection of the claims under 35 U.S.C. 103.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."** Also attached is a clean set of all pending claims for ease of reference.

CONCLUSION

Applicants respectfully request that the foregoing

amendments be considered and entered in the file history of the above-identified application. It is submitted that the claims are now in condition for allowance. It is therefore earnestly solicited that such a final favorable disposition is made. The Examiner is invited to telephone Jeffrey S. Kubinec, (Reg. No. 36,575) at (650) 225-8228 if deemed helpful to clarify and advance prosecution.

Respectfully submitted,
GENENTECH, INC.

Date: December 18, 2001 By: _____
Jeffrey S. Kubinec
Reg. No. 36,575
Telephone No. (650)225-8228

"Version with Markings to Show Changes Made"

In the claims:

Claim 1 has been amended as follows:

1. (twice amended) A [composition comprising a] substantially homogenous glycoprotein preparation, said glycoprotein having an immunoglobulin CH2 domain said CH2 domain having at least one N-linked oligosaccharide wherein [substantially all of] the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing a G1 and [or] G0 oligosaccharide in the preparation does not exceed 10% by weight of the preparation.